UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,215	03/04/2002	Adrienne Elizabeth Dubin	ORT-1601	5197

7590 12/23/2004

Philip S. Johnson, Esq.
Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003

EXAMINER	
LOCKARD, JON MCCLELLAND	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/090,215	DUBIN ET AL.	
	Examiner	Art Unit	
	Jon M Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 March 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/4/02, 10/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Alignment*.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Jon Lockard.

2. Claims 11 and 23 are pending.

3. The previous examiner indicated allowable subject matter in an Interview on 21 October 2004. Allowability is withdrawn. Rejections are applied below.

Information Disclosure Statement

4. The Information Disclosure Statements (IDS) submitted on 04 March 2002 and 12 October 2004 have been considered by the Examiner.

Drawings

5. Applicants are advised that upon issuance of a patent, the complete text of the sequence listing submitted in compliance with 37 C.F.R.§§1.821-1.825 will be published as part of the patent. Therefore, it is unnecessarily redundant to repeat the sequence information in the form of Figures. Applicants should amend the specification to delete any Figures (e.g. Figures 1-8, for example) which consist only of nucleic acid or protein sequences which have been submitted in their entirety in computer readable format (i.e. as SEQ ID NO:'s) and should further amend the specification accordingly to reflect the replacement of the Figure by the appropriate SEQ ID NO.

Specification

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Human vanilloid receptor VR3 protein".

Claim Rejections - 35 USC § 101 and 35 USC §112

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
>
> The following is a quotation of the first paragraph of 35 U.S.C. 112:
>
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 11 and 23 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility. Novel biological molecules lack an established utility and must undergo extensive experimentation to determine an appropriate specific, substantial, and credible utility.

10. The instant application discloses a polypeptide set forth as SEQ ID NO:12. The Specification teaches that SEQ ID NO:12 is one of three isoforms of the putative human vanilloid receptor identified as VR3A+B+ (See page 7, lines 26-27). The specification asserts that predicted amino acid sequence of VR3A+B+ set forth as SEQ ID NO:12 displays sequence homology and structural homology to the vanilloid receptor family (VR1 and VR2) (See page 8,

lines 15-20 and page 49, line 28 – page 50, line 6). The only experimental data or information provided by the Instant Specification on whether the putative VR3A+B+ protein (SEQ ID NO:12) functions like an ion channel is the disclosure that oocytes injected with VR3A+B+ RNA demonstrated enhancement of a heat-induced response (measured by whole cell currents) compared to controls (See Figure 10, page 5, line 17 – page 6, line 15). However, mere homology and a showing of increased responsiveness to heat would not be accepted by those of skill in the art as being predictive of function. For example, the Specification teaches that VR1 is activated by capsaicin and RTX, and activation of VR1 is blocked by the antagonists capsazepine and ruthenium red (See page 1, line 28 – page 2, line 2). However, the Instant Specification discloses that oocytes injected with VR3A+B+ RNA (encoding the claimed protein of SEQ ID NO:12) demonstrated no detectable differences in membrane conductance when compared to controls when challenged with a variety of ligands (including capsaicin and RTX), low pH, and depolarizing as well as hyperpolarizing voltage steps (See page 41, lines 22-25, Table 1). Therefore, the Specification's assertion that SEQ ID NO:12 functions as member of the vanilloid receptor family is not a substantial assertion of utility, since significant further research would be required of the skilled artisan to determine the function and/or biological activity of the putative receptor. There is no well-established utility for a specific nucleic acid or amino acid sequence, and the specification fails to disclose a specific and substantial utility for the claimed invention.

11. The specification asserts the following as patentable utilities for the claimed VR3 receptor protein (SEQ ID NO:12):

1) useful to identify modulators of the VR3 receptor (pg 3, lines 19-20);

2) identify agonists and antagonists (pg 4, lines 1-2);

3) production of antibodies (pg 22, line 4 – pg 25, line 8); and

4) pharmaceutical compositions as therapeutics (pg 27, line 5 – pg 32, line 29);

12. These asserted utilities are neither specific nor substantial because they do not identify or reasonably confirm a "real world" context of use. The specification neither identifies the biological functions of the claimed protein, nor any diseases that are associated with the claimed molecules. Without any biological activity or link to a disease, further research would be required to determine the properties of the claimed VR3 protein of SEQ ID NO:12 or to identify a disease that can be treated or diagnosed with the claimed molecules, which is insufficient to meet the requirement of 35 USC § 101.

13. These activities and functions are conjectural and are based solely on the identification of the putative protein of SEQ ID NO:12 as being a vanilloid receptor. While it is credible that SEQ ID NO:12 is a member of the TRP/vanilloid family of ion channels, its identification as such is not sufficient to establish either a well known, or a specific, substantial and credible utility. The negative results of the functional assays presented in the Specification are not indicative of any function, and no disease or disorder is correlated with the polypeptide. The use of a putative ion channel to discover its biological properties does not constitute a specific, substantial utility, but rather is further experimentation to determine the properties of that which is being claimed

14. The art teaches that the TRP/vanilloid family is large and there is no unifying theme to their function or mechanism of activation. Furthermore, members of the TRP family are widely distributed across a range of cell types, making it difficult to express confirmed monomeric channels, and several TRPs are known to form heteromulitmers and their electrophysiological

properties depend on the subunit composition. (Clapham et al. [2001]. Nature Reviews Neuroscience 2:387-396). Furthermore, the Specification of the Instant Application discloses that "although these novel nucleic acids and proteins display some sequence and structural homology to the TRP and vanilloid families of cation channel proteins as well as other cation channel proteins known in the art, it is also known in the art that proteins displaying such homologies have significant differences in function, such as conductance and permeability, as well as differences in tissue expression." Thus, although the homology of the TRP/vanilloid family, especially in the 6 transmembrane domain regions containing a short hydrophobic stretch between transmembrane regions 5 and 6, allows identification of such as both TRPs and as being evolutionarily related, such is not predictive of function. It is possible that, after further characterization, this protein might be found to have a patentable utility, in which case proteins would have a specific utility, or the protein might be found to be associated with a specific disease.

15. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct., 1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a protein which has undetermined function or

biological significance. Until some actual and specific activity or significance can be attributed to the protein identified in the specification as SEQ ID NO:12, the claimed invention is incomplete.

16. Claims 11 and 23 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to make/use the claimed invention.

Claim Rejections - 35 USC § 112, 2nd paragraph

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 11 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

19. Claim 11 is indefinite for reciting "an amino acid sequence set forth in SEQ ID NO:12" in line 2 of the claim. Without knowing whether the indefinite article "an" is intended to mean "the amino acid sequence of SEQ ID NO:12" or any portion of the amino acid set forth as SEQ ID NO:12, the metes and bounds of the claim cannot be determined.

20. Claim 23 is indefinite because it is not clear whether "has" means "comprises, in which case the claim is not further limiting, or "consists of". Amendment to the claim to use the more precise "consists of" is suggested.

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

22. Claim 11 is rejected under 35 U.S.C. 102(e) as being anticipated by Masters et al. (WO 01/34805, published 17 May 2201; priority date 12 November 1999).

23. Masters et al. teach a polypeptide set forth as SEQ ID NO:3 (See Figure 8) that comprises an amino acid sequence that shares 100% identity with residues 1-736 of SEQ ID NO:12 of the Instant Application (See attached sequence alignment). It is noted that the term "comprising an amino acid sequence", as recited in the claim is open language reading on a fragment, and thus the claim reads on the polypeptide taught by Maters et al. (See also 112¶2 rejections *supra*). Thus, the reference of Masters et al. meets all the limitations of claim 11.

Summary

24. No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback, Ph.D.** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
December 16, 2004

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

```
Qy          1 MADSSEGPRAGPGEVAELPGDESGTPGGEAFPLSSLANLFEGEDGSLSPSPADASRPAGP 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MADSSEGPRAGPGEVAELPGDESGTPGGEAFPLSSLANLFEGEDGSLSPSPADASRPAGP 60

Qy         61 GDGRPNLRMKFQGAFRKGVPNPIDLLESTLYESSVVPGPKKAPMDSLFDYGTYRHHSSDN 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GDGRPNLRMKFQGAFRKGVPNPIDLLESTLYESSVVPGPKKAPMDSLFDYGTYRHHSSDN 120

Qy        121 KRWRKKIIEKQPQSPKAPAPQPPPILKVFNRPILFDIVSRGSTADLDGLLPFLLTHKKRL 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 KRWRKKIIEKQPQSPKAPAPQPPPILKVFNRPILFDIVSRGSTADLDGLLPFLLTHKKRL 180

Qy        181 TDEEFREPSTGKTCLPKALLNLSNGRNDTIPVLLDIAERTGNMREFINSPFRDIYYRGQT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 TDEEFREPSTGKTCLPKALLNLSNGRNDTIPVLLDIAERTGNMREFINSPFRDIYYRGQT 240

Qy        241 ALHIAIERRCKHYVELLVAQGADVHAQARGRFFQPKDEGGYFYFGELPLSLAACTNQPHI 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 ALHIAIERRCKHYVELLVAQGADVHAQARGRFFQPKDEGGYFYFGELPLSLAACTNQPHI 300

Qy        301 VNYLTENPHKKADMRRQDSRGNTVLHALVAIADNTRENTKFVTKMYDLLLLKCARLFPDS 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 VNYLTENPHKKADMRRQDSRGNTVLHALVAIADNTRENTKFVTKMYDLLLLKCARLFPDS 360

Qy        361 NLEAVLNNDGLSPLMMAAKTGKIGIFQHIIRREVTDEDTRHLSRKFKDWAYGPVYSSLYD 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 NLEAVLNNDGLSPLMMAAKTGKIGIFQHIIRREVTDEDTRHLSRKFKDWAYGPVYSSLYD 420

Qy        421 LSSLDTCGEEASVLEILVYNSKIENRHEMLAVEPINELLRDKWRKFGAVSFYINVVSYLC 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 LSSLDTCGEEASVLEILVYNSKIENRHEMLAVEPINELLRDKWRKFGAVSFYINVVSYLC 480

Qy        481 AMVIFTLTAYYQPLEGTPPYPYRTTVDYLRLAGEVITLFTGVLFFFTNIKDLFMKKCPGV 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 AMVIFTLTAYYQPLEGTPPYPYRTTVDYLRLAGEVITLFTGVLFFFTNIKDLFMKKCPGV 540

Qy        541 NSLFIDGSFQLLYFIYSVLVIVSAALYLAGIEAYLAVMVFALVLGWMNALYFTRGLKLTG 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 NSLFIDGSFQLLYFIYSVLVIVSAALYLAGIEAYLAVMVFALVLGWMNALYFTRGLKLTG 600

Qy        601 TYSIMIQKILFKDLFRFLLVYLLFMIGYASALVSLLNPCANMKVCNEDQTNCTVPTYPSC 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 TYSIMIQKILFKDLFRFLLVYLLFMIGYASALVSLLNPCANMKVCNEDQTNCTVPTYPSC 660

Qy        661 RDSETFSTFLLDLFKLTIGMGDLEMLSSTKYPVVFIILLVTYIILTFVLLLNMLIALMGE 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 RDSETFSTFLLDLFKLTIGMGDLEMLSSTKYPVVFIILLVTYIILTFVLLLNMLIALMGE 720

Qy        721 TVGQVSKESKHIWKLQ 736
              ||||||||||||||||
Db        721 TVGQVSKESKHIWKLQ 736
```

* RESULT 3
AAE01227
ID AAE01227 standard; protein; 871 AA.
XX
AC AAE01227;
XX
DT 31-JUL-2001 (first entry)
XX
DE Human vanilloid receptor 3 (hVR3) protein.
XX
KW Human; vanilloid receptor 3; VR3; inflammation; arthritis; psoriasis;
KW wound healing; analgesic; vulnerary; antiallergic; gene therapy;
KW neuropathic pain; rhinitis; pruritus; bladder dysfunction;
KW cluster headache; capsaicin-sensitive ion channel disorder.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Domain 238. .269
FT /label= Ankaryn_repeat
FT Domain 284. .316
FT /label= Ankaryn_repeat
FT Domain 369. .402
FT /label= Ankaryn_repeat
FT Domain 470. .491
FT /label= Transmembrane_domain
FT Domain 515. .535
FT /label= Transmembrane_domain
FT Domain 551. .570
FT /label= Transmembrane_domain
FT Domain 575. .593
FT /label= Transmembrane_domain
FT Domain 617. .635
FT /label= Transmembrane_domain
FT Region 667. .681
FT /label= Poor_loop_region
FT Domain 693. .720
FT /label= Transmembrane_domain
XX
PN WO200134805-A2.
XX
PD 17-MAY-2001.
XX
PF 10-NOV-2000; 2000WO-US031077.
XX
PR 12-NOV-1999; 99US-00438997.
XX
PA (ABBO) ABBOTT LAB.
XX
PI Masters JN, Vos MH;
XX
DR WPI; 2001-335930/35.
DR N-PSDB; AAD05107.
XX
PT Novel human vanilloid receptor gene and encoded polypeptides for
PT identifying compounds that modulate vanilloid receptors in human tissues
PT and for treating inflammation, arthritis, psoriasis and wound healing.
XX
PS Claim 18; Fig 8; 91pp; English.
XX
CC The present sequence is human vanilloid receptor 3 (hVR3) protein.
CC Vanilloid receptor protein and its DNA are useful for identifying
CC compounds which modulate vanilloid receptors in human tissues, which are
CC useful for treating various disease states, including neuropathic pain,
CC inflammation, arthritis, rhinitis, pruritus, bladder dysfunction, cluster
CC headache, wound healing and psoriasis. Vanilloid receptor DNA is useful
CC as standard or reagent in diagnostic immunoassays, as targets for
CC pharmaceutical screening assays and also in gene therapy. Vanilloid
CC receptor protein is useful for detecting the presence of anti-vanilloid
CC receptor derived polypeptide in test samples. Vanilloid receptor
CC antibodies are useful for detecting vanilloid receptor polypeptides, for
CC screening for diseases or conditions associated with abnormal vanilloid
CC receptor production, treating disorders involving capsaicin-sensitive ion
CC channels and as diagnostic markers
XX
SQ Sequence 871 AA;

Query Match 99.2%; Score 3829; DB 4; Length 871;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 736; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 MADSSEGPRAGPGEVAELPGDESGTPGGEAFPLSSLANLFEGEDGSLSPSPADASRPAGP 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MADSSEGPRAGPGEVAELPGDESGTPGGEAFPLSSLANLFEGEDGSLSPSPADASRPAGP 60

Qy         61 GDGRPNLRMKFQGAFRKGVPNPIDLLESTLYESSVVPGPKKAPMDSLFDYGTYRHHSSDN 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GDGRPNLRMKFQGAFRKGVPNPIDLLESTLYESSVVPGPKKAPMDSLFDYGTYRHHSSDN 120

Qy        121 KRWRKKIIEKQPQSPKAPAPQPPPILKVFNRPILFDIVSRGSTADLDGLLPFLLTHKKRL 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 KRWRKKIIEKQPQSPKAPAPQPPPILKVFNRPILFDIVSRGSTADLDGLLPFLLTHKKRL 180
```

```
Qy        181 TDEEFREPSTGKTCLPKALLNLSNGRNDTIPVLLDIAERTGNMREFINSPFRDIYYRGQT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 TDEEFREPSTGKTCLPKALLNLSNGRNDTIPVLLDIAERTGNMREFINSPFRDIYYRGQT 240

Qy        241 ALHIAIERRCKHYVELLVAQGADVHAQARGRFFQPKDEGGYFYFGELPLSLAACTNQPHI 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 ALHIAIERRCKHYVELLVAQGADVHAQARGRFFQPKDEGGYFYFGELPLSLAACTNQPHI 300

Qy        301 VNYLTENPHKKADMRRQDSRGNTVLHALVAIADNTRENTKFVTKMYDLLLLKCARLFPDS 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 VNYLTENPHKKADMRRQDSRGNTVLHALVAIADNTRENTKFVTKMYDLLLLKCARLFPDS 360

Qy        361 NLEAVLNNDGLSPLMMAAKTGKIGIFQHIIRREVTDEDTRHLSRKFKDWAYGPVYSSLYD 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 NLEAVLNNDGLSPLMMAAKTGKIGIFQHIIRREVTDEDTRHLSRKFKDWAYGPVYSSLYD 420

Qy        421 LSSLDTCGEEASVLEILVYNSKIENRHEMLAVEPINELLRDKWRKFGAVSFYINVVSYLC 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 LSSLDTCGEEASVLEILVYNSKIENRHEMLAVEPINELLRDKWRKFGAVSFYINVVSYLC 480

Qy        481 AMVIFTLTAYYQPLEGTPPYPYRTTVDYLRLAGEVITLFTGVLFFFTNIKDLFMKKCPGV 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 AMVIFTLTAYYQPLEGTPPYPYRTTVDYLRLAGEVITLFTGVLFFFTNIKDLFMKKCPGV 540

Qy        541 NSLFIDGSFQLLYFIYSVLVIVSAALYLAGIEAYLAVMVFALVLGWMNALYFTRGLKLTG 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 NSLFIDGSFQLLYFIYSVLVIVSAALYLAGIEAYLAVMVFALVLGWMNALYFTRGLKLTG 600

Qy        601 TYSIMIQKILFKDLFRFLLVYLLFMIGYASALVSLLNPCANMKVCNEDQTNCTVPTYPSC 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 TYSIMIQKILFKDLFRFLLVYLLFMIGYASALVSLLNPCANMKVCNEDQTNCTVPTYPSC 660

Qy        661 RDSETFSTFLLDLFKLTIGMGDLEMLSSTKYPVVFIILLVTYIILTFVLLLNMLIALMGE 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 RDSETFSTFLLDLFKLTIGMGDLEMLSSTKYPVVFIILLVTYIILTFVLLLNMLIALMGE 720

Qy        721 TVGQVSKESKHIWKLQ 736
              ||||||||||||||||
Db        721 TVGQVSKESKHIWKLQ 736
```

```
RESULT 4
AAG65787
ID   AAG65787 standard; protein; 871 AA.
XX
AC   AAG65787;
XX
DT   30-JAN-2002  (first entry)
XX
DE   Human ion channel VR-5 protein sequence.
XX
KW   Ion channel; vanilloid receptor; VR-3; VR-5; nootropic; neuroprotective;
KW   antiparkinsonian; analgesic; antidiabetic; antiproliferative; cytostatic;
KW   antirheumatic; antiarthritic; gene therapy; antisense therapy.
XX
OS   Homo sapiens.
XX
PN   WO200168857-A2.
XX
PD   20-SEP-2001.
XX
PF   15-MAR-2001; 2001WO-US008329.
XX
PR   15-MAR-2000; 2000US-00525420.
XX
PA   (MILL-) MILLENNIUM PHARM INC.
XX
PI   Curtis RAJ,  Cook WJ;
XX
DR   WPI; 2001-596911/67.
DR   N-PSDB; AAI66972, AAI66973.
XX
PT   Nucleic acid encoding human ion channels referred to as Vanilloid
PT   receptor 3 (VR-3) and VR-5, useful for screening modulators of VR-3 or VR
PT   -5 and for treating calcium homeostasis related disorders (e.g. dementia)
PT   and pain disorders.
XX
PS   Claim 13; Fig 2A-C; 167pp; English.
XX
CC   The invention provides nucleic acid encoding human ion channels referred
CC   to as Vanilloid receptor 3 (VR-3) and VR-5. The VR-3 or VR-5 proteins can
CC   be used to screen for naturally occurring VR-3 or VR-5 ligands or for
CC   drugs or compound which modulate VR-3 or VR-5 activity. The VR-3 or VR-5
CC   proteins and their modulators (e.g. antisense nucleic acids and anti-VR
CC   antibodies) are useful for treating disorders characterized by
CC   insufficient or excessive production of VR-3 or VR-5. These disorders are
CC   calcium homeostasis related disorders (Alzheimer's disease, dementia,
CC   Parkinson's disease), pain disorders (diabetic neuropathy, rheumatoid
CC   arthritis) and/or cellular growth and/or proliferation disorders (e.g.
CC   cancer). Numerous other examples of these disorders are given in the
CC   specification. The present sequence represents the human VR-5
XX
SQ   Sequence 871 AA;
```

```
  Query Match           99.2%;  Score 3829;  DB 4;  Length 871;
  Best Local Similarity  100.0%;  Pred. No. 0;
  Matches  736;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MADSSEGPRAGPGEVAELPGDESGTPGGEAFPLSSLANLFEGEDGSLSPSPADASRPAGP 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MADSSEGPRAGPGEVAELPGDESGTPGGEAFPLSSLANLFEGEDGSLSPSPADASRPAGP 60

Qy         61 GDGRPNLRMKFQGAFRKGVPNPIDLLESTLYESSVVPGPKKAPMDSLFDYGTYRHHSSDN 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GDGRPNLRMKFQGAFRKGVPNPIDLLESTLYESSVVPGPKKAPMDSLFDYGTYRHHSSDN 120

Qy        121 KRWRKKIIEKQPQSPKAPAPQPPPILKVFNRPILFDIVSRGSTADLDGLLPFLLTHKKRL 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 KRWRKKIIEKQPQSPKAPAPQPPPILKVFNRPILFDIVSRGSTADLDGLLPFLLTHKKRL 180

Qy        181 TDEEFREPSTGKTCLPKALLNLSNGRNDTIPVLLDIAERTGNMREFINSPFRDIYYRGQT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 TDEEFREPSTGKTCLPKALLNLSNGRNDTIPVLLDIAERTGNMREFINSPFRDIYYRGQT 240

Qy        241 ALHIAIERRCKHYVELLVAQGADVHAQARGRFFQPKDEGGYFYFGELPLSLAACTNQPHI 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 ALHIAIERRCKHYVELLVAQGADVHAQARGRFFQPKDEGGYFYFGELPLSLAACTNQPHI 300

Qy        301 VNYLTENPHKKADMRRQDSRGNTVLHALVAIADNTRENTKFVTKMYDLLLLKCARLFPDS 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 VNYLTENPHKKADMRRQDSRGNTVLHALVAIADNTRENTKFVTKMYDLLLLKCARLFPDS 360

Qy        361 NLEAVLNNDGLSPLMMAAKTGKIGIFQHIIRREVTDEDTRHLSRKFKDWAYGPVYSSLYD 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 NLEAVLNNDGLSPLMMAAKTGKIGIFQHIIRREVTDEDTRHLSRKFKDWAYGPVYSSLYD 420

Qy        421 LSSLDTCGEEASVLEILVYNSKIENRHEMLAVEPINELLRDKWRKFGAVSFYINVVSYLC 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 LSSLDTCGEEASVLEILVYNSKIENRHEMLAVEPINELLRDKWRKFGAVSFYINVVSYLC 480

Qy        481 AMVIFTLTAYYQPLEGTPPYPYRTTVDYLRLAGEVITLFTGVLFFFTNIKDLFMKKCPGV 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 AMVIFTLTAYYQPLEGTPPYPYRTTVDYLRLAGEVITLFTGVLFFFTNIKDLFMKKCPGV 540

Qy        541 NSLFIDGSFQLLYFIYSVLVIVSAALYLAGIEAYLAVMVFALVLGWMNALYFTRGLKLTG 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 NSLFIDGSFQLLYFIYSVLVIVSAALYLAGIEAYLAVMVFALVLGWMNALYFTRGLKLTG 600

Qy        601 TYSIMIQKILFKDLFRFLLVYLLFMIGYASALVSLLNPCANMKVCNEDQTNCTVPTYPSC 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 TYSIMIQKILFKDLFRFLLVYLLFMIGYASALVSLLNPCANMKVCNEDQTNCTVPTYPSC 660

Qy        661 RDSETFSTFLLDLFKLTIGMGDLEMLSSTKYPVVFIILLVTYIILTFVLLLNMLIALMGE 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 RDSETFSTFLLDLFKLTIGMGDLEMLSSTKYPVVFIILLVTYIILTFVLLLNMLIALMGE 720
```